

**69th Meeting of the National Cancer Institute (NCI)
NCI Council of Research Advocates (NCRA)
National Institutes of Health (NIH)**

Update on Precision Medicine

**Building 31, C Wing, Conference Room 6
NIH Campus
Bethesda, Maryland**

October 19–20, 2015

Members Present

Mr. David Arons, Chair
Dr. Gregory H. Aune
Mr. William Bro
Dr. Sue Friedman
Ms. Shelley Fuld Nasso

Ms. Martha Gaines
Dr. June McKoy
Ms. Kimberly Newman-McCown
Ms. Heather Ortner
Mr. Roberto Vargas

Speakers

Dr. Jeffrey S. Abrams, Acting Director for Clinical Research, Associate Director of the Cancer Therapy Evaluation Program (CTEP), Division of Cancer Treatment and Diagnosis (DCTD), NCI

Mr. David Arons, Chair, NCRA; Interim Chief Executive Office, National Brain Tumor Society

Dr. Barbara A. Conley, Associate Director, Cancer Diagnosis Program, DCTD, NCI

Ms. Andrea Denicoff, Nurse Consultant, Clinical Investigations Branch, CTEP, DCTD, NCI

Ms. Holly Gibbons, Program Analyst, Office of Government and Congressional Relations, NCI

Ms. Joya Delgado Harris, Director, Office of Research Integration, American Cancer Society; co-chair, Advocate Engagement Working Group (AEWG), NCRA, NCI

Dr. Lee J. Helman, Senior Investigator, Pediatric Oncology Branch; Head, Molecular Oncology Section; Acting Director, Center for Cancer Research (CCR) and CCR Scientific Director for Clinical Research, NCI

Dr. Katherine L. Hudson, Deputy Director for Science, Outreach, and Policy, NIH

Dr. Douglas R. Lowy, Acting Director, NCI; Chief, Laboratory of Cellular Oncology, NCI

Dr. Richard E. Manrow, Senior Advisor, Science and Policy, Office of Communications and Public Liaison, NCI

Dr. Sanya A. Springfield, Director, Center to Reduce Cancer Health Disparities, NCI

Ms. Cynthia Meals Vitelli, Associate Director, Office of Public Affairs, Office of Communications and Public Liaison, NCI

Ms. Amy Williams, Acting Director, Office of Advocacy Relations (OAR); Executive Secretary, NCI Council of Research Advocates, NCI

Facilitator
Dr. Clifford Goodman

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Day 1: Monday, October 19, 2015

Welcome and Opening Remarks

Dr. Goodman, Mr. Arons, Ms. Williams

- Dr. Goodman, Mr. Arons, and Ms. Williams welcomed NCRA members and guests, including alumni. The agenda covers precision medicine, the work of the advocacy office, and networking activities, with considerable discussion time built in.
- NCRA members, NCI staff, and presenters introduced themselves.
- Ms. Williams explained that OAR has been in a transition period and is restructuring to reflect the heterogeneity of the advocacy community. It will split its efforts between work with advocates on a personal level and work with advocates on an organizational level.

NCI Update

Dr. Lowy

- NCI bases its judgment about annual funding needs on current cancer trends.
- Cancer death rates are declining; from 1990 to 2012, the overall cancer death rate in the United States fell by 23 percent.
- Unfortunately, for some cancers and among some populations, the incidence is increasing.
 - In 2012, the incidence of colorectal cancer was 22 percent higher in African Americans compared to the general population.
 - By 2030, worldwide cancer cases are expected to increase by 52 percent and worldwide cancer deaths will increase by 61 percent, largely due to an aging population and increasing life expectancy. Most of the increases in deaths are in the developing world.
- The NCI budget has been flat and subject to a decade of decreasing purchasing power. This makes it difficult to sustain research.
- The President's FY16 budget appropriation proposal for NCI requested a \$145 million increase, with \$70 million of the increase for the Precision Medicine Initiative (PMI) oncology portion (PMI-O). Each house of Congress has passed somewhat different bills that support increases for NCI.
- NCI's FY17 budget proposal, available at <http://www.cancer.gov/about-nci/budget/plan>, provides a snapshot of where cancer research is today and how scientific opportunities can flourish in the years ahead.
- NCI is proposing a budget increase of 7 percent for 2017, with a sustained increase of 7 percent per year, which would lead to a doubling over the next 10 years.
- The NCI's Precision Medicine Initiative is comprised of four components:
 1. Developing and expanding clinical therapy trials in precision oncology.
 2. Improving predictive oncology by overcoming drug resistance and determining effective combination targeted therapy.
 3. Creating a new array of laboratory models to increase understanding of cancer biology.
 4. Building a national cancer knowledge system that integrates cancer genomic information, clinical information, and laboratory model information.

- NCI priorities include investigator-initiated research, understanding and overcoming disparities, developing support for the research infrastructure, and expanding precision medicine beyond treatment to also encompass cancer screening and prevention.
- Partnerships and collaborations are essential for NCI to make progress against cancer. Advocates can help build bridges, bring experts together, and leverage funding.
- The funding rate for applications (about 13 percent) can be discouraging for young investigators.
- NCI is trying to recruit minorities, both for the workforce and for trial enrollment.

Precision Medicine Initiative—NIH Perspectives and Plans

Dr. Hudson

- Dr. Hudson co-chairs the PMI Cohort Program working group, a multidisciplinary group of patient advocates, geneticists, computational experts, and researchers who brought together divergent ideas to design a plan to move the country into an era when medical treatment can be tailored to the individual patient.
- The working group conducted a survey of a representative sample of the population's views of the proposed cohort sample, concerns, and expectations.
- The general concept of the cohort is to enroll 1 million or more volunteers who represent the diversity of the country, collect biospecimens and other information, and follow the volunteers for many years, expanding the study over the years with new technology. An emphasis is on self-reported information from mobile devices. Social media also will play a role.
- Funding for the cohort will begin in 1 year. Dr. Hudson would like to accelerate this.
- NIH is working on building programs and categorizing information to maximize use of electronic health records.
- NIH has a PMI website (<http://www.nih.gov/precisionmedicine>) that provides background about the program.
- Advocates were involved in planning the PMI Cohort Program and will continue to have a role to play, particularly in recruiting underrepresented minorities. Children also will be represented.

NCI's Precision Medicine Initiative for Oncology

Dr. Abrams

- Precision medicine consists of interventions to prevent, diagnose, or treat a disease (e.g., cancer), based on a molecular and/or mechanistic understanding of the causes, pathogenesis, and/or pathology of the disease.
- When the individual characteristics of patients are sufficiently distinct, precision medicine interventions can be concentrated on those who will benefit, sparing expenses and side effects for those who will not.
- Current work usually involves biopsying, but a goal is to use less invasive imaging.
- NCI Precision Medicine initiative will expand genomics-based clinical trials and work to understand and overcome resistance to targeted drugs and drug combinations. It also will provide a mechanistic understanding of immunotherapy.

- To advance understandings, NCI's precision medicine initiative will build a repository of patient-derived preclinical models for evaluating targeted therapeutics and a national cancer database to integrate genomic information with clinical responses and outcomes.
- Four Precision Medicine (PM) trials were launched in 2014:
 - The Molecular Profiling-based Assignment of Cancer Therapeutics (M-PACT) trial is trying to assess whether treatment based on genetic screening can improve the rate and duration of response in patients with advanced solid tumors.
 - The Lung Cancer Master Protocol (Lung-MAP) is a broad partnership that uses a multidrug, targeted screening approach to match lung cancer patients with sub-studies testing investigational new treatments based on genomic alterations that drive the growth of their cancer.
 - The Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trials (ALCHEMIST) are a group of clinical trials for patients with certain types of early-stage non-small-cell lung cancer (NSCLC) that has been treated surgically.
 - The Exceptional Responders Initiative examines patients who have a unique, encouraging response to treatments that are not effective for most other patients. There are more than 450 patients, and it is enrolling rapidly, with considerable patient and investigator interest. The goal is to enroll 3,000 patients. The hope is that exceptional responders can lead to better outcomes for a large number of patients.
- A fifth PM, NCI Molecular Analysis for Therapy Choice (NCI-MATCH), was launched in 2015. It assigns therapy based on molecular abnormalities, not site of tumor origin, for patients without available standard therapy. The study is enrolling about 65 patients per week.
 - In NCI-MATCH, after a study agent is administered, patients will be monitored for stable disease, complete or partial response, or progressive disease.
 - Treatments will be considered promising for incorporating into future studies if at least 16 percent of the patients in an arm are observed to have tumor shrinkage.
 - A pediatric counterpart to NCI-MATCH will enroll children with advanced cancers who have not progressed on standard therapy and explore treating them based on the molecular profiles of their tumors.
- The vision for the National Clinical Trials Network (NCTN) is innovative science that answers questions the private sector might not address. NCI-MATCH is a good first example. NCTN will be able to reach special populations such as minorities, patients with rare tumors and uncommon subsets of common tumors, and community practices.
- Precision medicine techniques also will focus on learning more about mechanisms of resistance to targeted cancer therapeutics. NCI is creating a national repository of patient-derived models that will assess tumors that have been particularly difficult to treat.
- The new Cancer Genomics Data Commons will bring data together and serve as a single repository for all NCI cancer genomics data.
- NCI hopes for input from the advocacy community to move precision medicine efforts forward.
- In discussion, the NCRA considered intellectual property rights and ownership of tissue, informed consent, drug affordability, adherence, and minority representation in trials.

Update from Advocate Engagement Working Group

Ms. Harris, Ms. Williams

- AEWG was formed to explore best practices related to the issue of advocates in research. Its priorities are to:
 - Identify and recruit research advocates to participate in NCI activities.
 - Engage research advocates in NCI activities.
 - Support research advocates.
- AEWG exists at a critical time for OAR and has been helpful as a sounding board for OAR.
- AEWG will explore opportunities to broaden NCI's pool of research advocates. It has identified cancer-focused national meetings that could be forums for OAR outreach and promotion of NCI advocacy opportunities.

Legislative Update

Ms. Gibbons

- The NCI Office of Government and Congressional Relations works closely with OAR and is very engaged with the efforts of cancer research advocacy.
- The goal of the office is to make material understandable and compelling.
- Dr. Lowy and other representatives of NCI leadership participate in Congressional hearings and similar activities.
- To replace the continuing resolution, NCI is hoping for an omnibus bill that will fund the Institute.
- Ms. Gibbons depends on her NCI colleagues to help make technical material understandable and then works primarily with congressional staffers.

NCI Precision Medicine Clinical Trials

Dr. Conley

- The idea of precision medicine has caught fire, but the trials remain works in progress.
 - ALCHEMIST is for adjuvant treatment of non-squamous NSCLC for patients who have already had local treatment such as surgery.
 - Three integrated trials are testing targeted therapy in early stage lung cancer to determine whether starting treatment early enhances its effect.
 - Treatment is based on genotype. Patients with epidermal growth factor receptor (EGFR) mutations are entered in a phase III trial of erlotinib versus placebo for 2 years, and patients with *ALK*-rearranged mutations are entered in a phase III trial of crizotinib versus placebo for 2 years.
 - Lung-MAP is for squamous lung cancer, which is decreasing in incidence as smoking decreases, but which is still a troublesome problem.
 - Lung-MAP is a private/public/government trial designed as randomized phase II trials that will then move on to a randomized phase III trial.
 - Based on the results of genomic screening, patients are assigned to whichever of five sub-studies testing different investigational treatments or standard care best suits their genomic profile.

- NCI-MATCH is not specific to any tumor.
 - The objective of NCI-MATCH is to understand the relative efficacy of the same therapy applied to oncogene-defined subsets across different tumor histologies.
 - The primary hypothesis is that tumors that share common somatic genetic alterations in oncogenes will be variably responsive to therapies targeting the oncogenic pathway based on lineage-specific factors.
 - NCI-MATCH will test 3,000 patients to find widely distributed genetic alterations in about 1,000 of them.
 - For each molecularly-defined arm, the primary endpoint is the overall response rate, with 25 percent seen as promising. Each arm will include approximately 35 evaluable patients.
 - Ten sub-studies were activated in August 2015. Seven new arms are expected to open in December 2015, and another five are expected to open in April 2016.
- The Exception Responders Initiative is a pilot phenotype-to-genotype study.
 - Exceptional responders represent the other side of the coin to MATCH.
 - The study will attempt to determine the molecular mechanisms of unexpected responses to drugs that are inactive in most patients.
 - NCI asked clinicians to propose exceptional responder cases.
- M-PACT is a pilot study, with less evidence than some of the other studies.
- Pediatric MATCH will be up and running as soon as possible.
- In discussion, participants raised questions about alternative medicine and a possible relation to exceptional responders, the effect of changes in funding on the trials, possible treatment toxicities, drug resistance, and marketing the treatments.

Day 1 Wrap-Up

- In discussion, participants addressed public understanding of precision medicine, why patients volunteer for clinical trials, and excitement about the prospects of precision medicine.
- Speakers have not addressed the relation of precision medicine to population-wide interventions.
- NCRA members expressed disappointment about funding deficiencies
- Another topic of interest is survivorship.
- Advocates would like to learn more specifics about how NCI can use their contributions.
- Health disparities are a continuing topic of interest.

Day 2: Tuesday, October 20, 2015

Opening; Reflections from Day 1

Dr. Goodman

- The day began with an informal meet-and-greet with NCI leaders and NCRA members.

- The main topics of Day 1 were the NCI budget, precision medicine, advocate engagement, NCI communications, and the need to address disparities and include underserved populations in trials.

Facilitated Discussions: *Perspectives on Enhancing and Improving Clinical Trial Accrual*

Dr. Goodman, Dr. Helman, Dr. Springfield, Ms. Denicoff

- Advocates play an important role for NCI. The Institute needs to know what people in the community want it to do.
- Most cancer research is inter-related. It cannot function in silos. Cancer researchers must work together rather than compete.
- Tackling disparities is important.
 - The field struggles with why some cancers affect minorities more than others.
 - Another struggle is the lack of diversity in the NCI workplace. Addressing that will help with an understanding of health disparities.
- An ethical dilemma is posed by patients who consent to genomic testing but then opt out of knowing the results.
- The functions of the Center to Reduce Health Disparities are to spawn disparity research across NCI and learn about biological and genetic differences in cancers, to address the underrepresentation of minorities in the workforce, and to integrate research with training, both intramural and extramural. Health disparities are much more than an access question.
 - The Center can partner with advocates through regional coordinators.
 - NCI could promote diversity in genetic counseling (e.g., Spanish-language counselors) by providing administrative supplements to grants that address disparities. Also, some regions have developed multiple resources in multiple languages, and the Center is trying to share these across regions.
- Ms. Denicoff said that one of her primary interests is accrual for trials, including increasing the population of underrepresented populations and minorities. Accrual issues relate to barriers at sites, and community physicians are involved to address those barriers. These are challenges that NCRA can work with NCI to address.
- Accrual can be difficult for some trials.
 - An example is proton versus photon treatment trials, which can be challenging to enroll, because some insurance companies do not cover the treatment.
 - The NCI Community Oncology Research Program offers a good model of site-level accrual.
 - Knowing where trials will be helps with achieving sufficient minority accrual. But the challenge is connecting from national groups to local communities.
 - Community health educators play a critical role.
- Patients should be treated at centers that offer options that include clinical trials. NCI must work with community outreach efforts to align treatment and trial enrollment goals.
- Education about clinical trials is needed for different populations to help accrual.
 - Health care providers need education. Doctors might be reluctant to refer patients to a trial because of what it means for their own income stream.
 - It is necessary to educate patients to know their tumors, their markers, and other things about their disease so that they will be equipped to find trials for which

they are eligible. Newly diagnosed patients, particularly underserved patients, might not know they have a marker that qualifies them for a trial. The best approach is to be treated at a center with a wide menu of choices.

- Advocates could disseminate lists of trials to their organizations' membership.

NCI Communication Strategies and Messaging: Bypass Budget and PMI

Ms. Vitelli, Dr. Manrow

- The Bypass Budget plan describes NCI goals and priorities.
- The FY16 NCI budget is approximately \$5.1 billion, and the total NCI FY17 budget recommendation is approximately \$5.4 billion. In the FY17 NCI budget, about half of funding is for basic science. Other major budget items are for prevention and early detection clinical trials, immunotherapy clinical trials, precision oncology, and cancer health disparities.
- Additional resources are requested for 2017 in two areas: understanding cancer and bringing cancer research to the public.
 - The understanding cancer category requests \$150 million to study cancer causes and disease progression, biology of cancer health disparities, biology of the immune system, and genomic analysis of tumors.
 - The bringing cancer research to the public category requests \$205 million for precision medicine clinical trials, additional treatment trials, translational research, prevention and early detection, and bioinformatics.
- NCI wants to make its budget document more than a piece of paper or a web post. The Institute is sponsoring a series of blogs related to the budget, with comment sections to allow feedback.
- To let people know about the budget document, the Office of Communications and Public Liaison used email blasts to Congress, NCI grantees, NCI staff, cancer centers, professional societies, and advocates, as well as posts on social media such as Facebook and Twitter.
 - The average time people spent on the budget web pages increased by 77 percent over last year.
 - The number of viewers of the budget table increased by 66 percent compared with last year.
- Precision medicine continues to be a priority for NCI.
 - The rollout of NCI-MATCH received very favorable media comments.
 - During the MATCH rollout, there were 8,300 web page views, 2,400 Twitter engagements, 2,600 emails sent to stakeholders, and 287 calls about MATCH to the NCI call center.
 - The two key PMI communications messages are:
 - To emphasize NCI's role in the President's PMI as instrumental in moving the concept of precision medicine into everyday clinical practice.
 - To encourage diverse populations to consider taking part in PMI clinical trials and to encourage the clinicians who serve them to refer their patients to NCI-sponsored precision medicine trials.
 - The Office of Communications has a four-pronged strategy for PMI: content development, media relations, digital and social media, and audience outreach.

- The Office would like to hear from NCRA members about how they and their constituents could use the Bypass Budget to communicate about cancer research priorities and understand the implications of changes.

Talking Basic Research and Cancer: Google Hang out with Dr. Lowy

- The NCRA took a break to participant in NCI's first Google Hangout, which featured Dr. Lowy, Acting Director, NCI and Dr. Tom Misteli, a senior investigator for NCI's Center for Cancer Research, answered questions about a variety of topics related to cancer research.

Open Discussion and Wrap-Up

Dr. Goodman and Council members

Dr. Goodman asked NCRA members to state the most important and actionable messages that came out of the meeting for them.

- Cancer survivors are an underserved population who should be addressed. Researchers must continue to study late effects of treatment.
- It is important for advocates to learn more about the basic science of cancer. Translating discovery is necessary not only in clinical science but also in policy and population science.
- Workforce diversity is important to help the workforce connect with diverse populations and explain the role of precision medicine so that minority populations can benefit from it. There is a need for more minority representation in research.
- Short-term ways to take actions could involve re-tweeting messages and sharing Facebook posts. A longer-term approach is to educate people about what clinical trials are and how they can benefit.
- Advocates need to present reasons when they ask elected officials for funding. Specifically, advocates should be prepared to discuss the value of basis research and the fact that instability of yearly funding makes it difficult for investigators to stay in or join the field.
- It is a very good time for this group, and meetings like this one represent the best of open government.
- Success requires money and drugs, but it also requires laying a foundation for future work. This group can and should go beyond basic federal advisory committee work, becoming involved with specific work on photons or protons, survivorship, enrollment, and accrual. There are many ways. Teleconferences between face-to-face meetings can help move ideas along.